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Case Report

Fatal Septic Shock with Presumed Urinary Source in a Patient with Clinically Suspected, Previously Undiagnosed Von Hippel–Lindau Disease: A Case Report and Literature Review

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ABSTRACT

Background: Von Hippel-Lindau disease is a rare form of autosomal dominant cancer syndrome that affects multiple organs, such as the retina and brain hemangioblastoma, renal disease, and other visceral malignancies. Delayed diagnosis is a significant reason for avoidable mortality and morbidity.
Case Presentation: We present a case of a 47-year-old male presenting with fever, vomiting, hypotension, and pus discharge from his urethral catheter, developing into septic shock with multiple organ dysfunction syndrome. He had several decades of progressive symptoms clinically compatible with possible VHL syndrome, consisting of bilateral blindness secondary to globe enucleations performed since childhood, multifocal spinal cord lesions resulting in quadriparesis and neurogenic bladder, and a family history of retinoblastoma, brain tumors, and renal lesions. MRI of the spine showed extensive multifocal intramedullary enhancing lesions, from the cervicomedullary junction to T11, associated with dilated cord due to cystic changes, compression of the posterior medulla leading to obstructive hydrocephalus, and an occipital lesion. These findings favored multiple spinal hemangioblastomas. A corticomedullary cyst of the right kidney was seen. Despite intensive supportive therapy and appropriate broad-spectrum antibiotics, he succumbed to septic shock complicated by a presumed urinary source on hospital day 4.
Conclusion: This particular case illustrates the potential of unidentified genetic tumors resulting in significant neurological problems and infections leading to death. Early detection of multifocal hemangioblastomas and retinal problems can lead to early identification of patients at risk of developing VHL disease.

1. Introduction

Von Hippel-Lindau syndrome is a rare autosomal dominant multiorgan neoplasm characterized by involvement of all races with a penetrance rate of nearly 100% by 65 years of age [1, 2]. The estimated prevalence rate is 1 out of 36,000 births. Its occurrence results from a mutation in the VHL gene, which encodes the VHL protein, discovered by Latif et al. in 1993 [3] and mapped to locus 3p25 – 26 on the short arm of chromosome 3. This protein plays an indispensable role in mediating the hypoxic pathway, in which, under normoxic conditions, it ubiquitinates the HIF-α subunit, leading to its proteasome-dependent degradation. Lack of the protein results in persistent HIF-α stabilization and increased levels of gene products associated with angiogenesis and mitosis, a mechanism that was awarded the Nobel Prize in Physiology or Medicine in 2019 [4].

VHL disease clinical presentation includes hemangioblastomas of the CNS and retina, clear cell RCC, renal cysts, pheochromocytomas/paragangliomas, endolymphatic sac tumors, pancreatic cysts/neuroendocrine tumors, and epididymal cystadenomas [5]. High phenotypic variability exists, even among individuals with the same germline mutations, with the average age at symptom onset ranging from 20 to 40 years [2, 6]. The diagnostic criteria for VHL disease were initially proposed by Melmon and Rosen (1964) and later modified. In patients without a family history, diagnosis requires two VHL lesions, with at least one being a hemangioblastoma, whereas a single lesion suffices in those with a positive family history [6, 7].

Misdiagnosis of the VHL syndrome is still considered an important cause of preventable morbidity and mortality due to the lack of recognition of early symptoms as markers of a hereditary condition affecting multiple organs of the body. In the current case presentation, a 47-year-old man was reported to have had a series of manifestations caused by VHL syndrome throughout several decades before dying from septic shock. Posthumous diagnosis of VHL syndrome in the current patient was suspected clinically in accordance with well-known criteria for this condition.

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2. Literature Review

2.1. Study Design and Data Extraction

The subsequent section highlights a review of the literature collected through a search of the PubMed and Google Scholar databases from inception until February 2026 utilizing the key terms "von Hippel-Lindau Disease," "VHL Hemangioblastoma," "Retinal Hemangioblastoma," "Spinal Hemangioblastoma," "VHL Renal Manifestations," and "VHL Diagnostic Criteria," with no date constraints applied. Additional sources were gathered from references cited within selected articles. This study is not a systematic or scoping review. Both research studies and systematic, narrative, or case reviews relevant to VHL syndrome were included.

2.2. Epidemiology and Genetics

VHL is an autosomal dominant genetic disorder characterized by high penetrance with a birth prevalence of 1 in 36,000 to 91,000 cases [1, 2]. Twenty percent of VHL patients harbor de novo mutations; therefore, the absence of family history cannot be used to rule out VHL [8]. Clinical penetrance reaches 90% by age 65 years, and symptoms become apparent between ages 10 and 30 years [2]. The gene alterations include missense, nonsense, frameshift, and large-deletion mutations. There is a phenotype-genotype correlation whereby adrenal mass development (VHL type 1) is unlikely with truncating mutations, and some missense mutations are predictive of pheochromocytoma (VHL types 2A, 2B, and 2C) [5, 9].

2.3. CNS Hemangioblastomas

The prevalence rate of CNS hemangioblastoma in VHL syndrome is between 60% and 80%. Hemangioblastomas in the central nervous system are grade I vascularized tumors that arise from stromal cells [10, 11]. The common sites in VHL-associated tumors are cerebellum (44-72%), spinal cord (14-50%), and brain stem [10, 12]. The onset of hemangioblastomas associated with VHL syndrome occurs earlier compared to sporadic tumors and also has a high incidence of multiple tumors [12]. The signs and symptoms of VHL-associated hemangioblastoma include progressive myelopathy with sensory and motor deficits, pain, and myeloradiculopathy; large hemangioblastomas may lead to significant syringomyelia [12, 13]. The presence of brainstem lesions in VHL-associated hemangioblastoma in the cervicomedullary region or posterior medulla causes obstruction of the fourth ventricle, resulting in hydrocephalus [14]. Surgical treatment is the standard treatment for VHL-associated CNS hemangioblastomas; timely treatment should be performed to avoid permanent disabilities [12]. Belzutifan, an inhibitor of HIF-2α, was FDA-approved in 2021 as the first pharmacological therapy for non-surgical VHL-associated CNS hemangioblastomas [15, 16].

2.4. Ocular Manifestations

Retinal hemangioblastomas occur in about 50% of patients with VHL, with presentation usually in the second decade of life, although cases below age 10 have been reported [17]. Retinal hemangioblastomas originate as highly vascular tumors with dilated supplying and draining vasculature in the retina: exudative changes, retinal traction, secondary glaucoma, and neovascularization cause retinal detachment and blindness. Bilateral involvement leading to enucleation is infrequent; however, a recent prospective cohort study of 406 patients with VHL found unilateral enucleation in 8.2% of cases [18]. Bilateral enucleation, as seen in the current patient, is rare and reflects the outcome of bilaterally severe retinal hemangioblastoma, complicated by end-stage glaucoma and phthisis bulbi secondary to an uncontrollable disease process [17, 18]. Lens dislocation is a non-classical VHL manifestation; however, in advanced stages of ocular disease, it is a mechanical effect of increased intraocular pressure.

2.5. Renal and Visceral Manifestations

The clear cell variant of RCC is seen in more than 70% of VHL patients and represents the most common reason for VHL-related deaths. In some studies, renal cysts, which may be either simple or complicated, have been reported in up to 60% of patients with or before the occurrence of an RCC. The average age of diagnosis for RCC in VHL patients is between 33 and 37 years [5]. One must bear in mind that simple renal cysts are often a coincidental finding in middle-aged individuals without VHL disease; thus, their interpretation should be evaluated within the clinical context before assigning any diagnostic relevance to VHL syndrome. Other visceral symptoms are adrenal pheochromocytomas, pancreatic cysts, and endolymphatic sac tumors.

2.6. Diagnostic Criteria and Screening

The criteria for VHL disease include the discovery of two or more hemangioblastomas, or of one hemangioblastoma with an organ manifestation in those lacking a family history [6, 7]. A solitary finding suffices in diagnosing the condition in individuals with positive family history. Multisystem surveillance, according to existing guidelines, should be instituted from early childhood among at-risk individuals. MRI of the brain and spine, ophthalmologic examination, abdominal imaging, and plasma/urine analysis for catecholamines form the recommended imaging studies [7]. Definitive genetic testing identifies the condition and helps conduct cascade testing among relatives [5]. In the current scenario, the presence of bilateral eye disease leading to bilateral enucleation, extensive segmental multifoci involvement of the spinal cord along with positive family history fits into the diagnostic criteria for VHL disease as defined by Melmon & Rosen (1964) and later modified by Binderup et al. (2022) [6, 7]; the sole limitation being the lack of histopathological or genetic evidence in support of these lesions.

3. Case Presentation

3.1. Patient History and Background

A 47-year-old man came to the ED with complaints of fever for five days and nausea with vomiting for one day. Multiple diseases complicated the patient's previous medical history throughout decades. He developed blindness in the left eye from childhood at the age of approximately ten years, which progressed to complete loss of vision and enucleation of the left eye. Whether the cause of blindness was retinal hemangioblastoma, which is the probable diagnosis on ophthalmic consultation, could not be confirmed because the pathological findings from the removed eye were unavailable. The right lens dislocated at approximately 20 years of age and recurred after 5 years, leading to removal of the lens and, subsequently, the entire globe of the right eye. Also, HCV infection was detected in his thirties **(Table 1)**.

There has been increasing quadriplegia for 3 years before admission, which eventually led to long-term urinary catheterization, indicative of developing neurogenic bladder dysfunction. There are no reports of neurological or spinal imaging studies during this period. About 20 days before the present presentation, there was a case of T3-T4 laminectomy with removal of a spinal space-occupying lesion due to a fall; however, the indication for the procedure, neurological examination, post-operative report, and pathology reports of the specimen removed are lacking. It cannot be confirmed whether a

Table 1: Presents a chronological summary of the patient's clinical course from childhood through the fatal admission. CARE-compliant clinical timeline.

Age (yr)	Approx. Year	Event	Investigation / Intervention	Outcome
~10	~1986	Sudden-onset left visual loss progressing to complete blindness	Ophthalmological evaluation; retinal diagnosis not documented as hemangioblastoma in available records	Left globe enucleation
~20	~1996	Right lens dislocation; Hepatitis C virus (HCV) diagnosis	Surgical lens correction; HCV confirmed (viral load, fibrosis staging, and treatment records unavailable)	Partial right visual preservation; HCV managed expectantly
~25	~2001	Recurrent right lens dislocation; progressive right visual decline	Surgical lens removal	Right globe enucleation; bilateral visual loss established
~44	~2020	Onset of progressive quadriparesis	No neurological investigation or spinal imaging documented from this period	Gradual decline to quadriplegia; urinary catheter dependence established
47	~Day −20	Fall; spinal lesion identified on prior imaging	T3–T4 laminectomy; excision of spinal space-occupying lesion; histopathology unavailable; preoperative vs postoperative neurological status undocumented	Postoperative course undocumented; catheter dependence continued
47	Day 0	5-day fever; 1-day nausea/vomiting; septic shock on arrival	ED presentation; orotracheal intubation; urethral catheterization (purulent output); ABG, CBC, coagulation screen; MRI brain and spine; abdominal USS. Urine/blood cultures and lactate unavailable.	Empiric piperacillin-tazobactam; norepinephrine initiated; ICU admission
47	Days 1–3	Refractory hemodynamic instability; escalating vasopressor requirements	Sequential addition of dobutamine and dopamine; standard dosing in mcg/kg/min unavailable (recorded as drops/min); MAP targets, fluid balance, ventilation parameters, and SOFA score not documented	Persistent septic shock; progressive multi-organ dysfunction
47	Day 4	Critical hemodynamic deterioration; terminal ABG: pH elevated, SpO_2 70%, bicarbonate elevated, base excess +5.5	Family declined CPR and further escalation; no post-mortem examination documented; germline VHL mutation testing not performed	Death from refractory septic shock and multi-organ failure; posthumous clinical diagnosis of clinically suspected VHL disease

ABG, arterial blood gas; CBC, complete blood count; CPR, cardiopulmonary resuscitation; ED, emergency department; HCV, hepatitis C virus; MAP, mean arterial pressure; MRI, magnetic resonance imaging; SOFA, Sequential Organ Failure Assessment; USS, ultrasound; VHL, von Hippel–Lindau.

urinary catheter was placed before the procedure or later, as a pre-existing neurogenic bladder was known; further, the type of catheter used and how long it was in place before admission are not known.

The family history, which was collected by interviewing the patient without corroborating information from medical records, revealed that the patient's younger sister had a right occipital brain tumor, the patient's older sister had vision impairment due to a brain tumor, and the patient's mother had a renal tumor. It was unknown whether any of the patient's relatives had ever been evaluated for cancer, genetic testing, or cascade testing. There was no documentation that the patient had ever attended genetic counseling or hereditary tumor screening programs.

3.2. Examination and Initial Investigation

On presentation, the patient was unstable with a heart rate of 130 beats per minute and blood pressure of 90/30 mmHg. The need to improve his clinical status led to orotracheal intubation and starting him on mechanical ventilation. The purulent discharge from the urethral catheter indicated a urinary infection. Results of the urinalysis, urine and blood cultures, and identification of the organism could not be obtained because these tests were not performed. Serum lactate and procalcitonin levels were not documented.

The laboratory tests revealed leukocytosis with neutrophilia, relative lymphopenia, and increased red cell distribution width. Increased activated partial thromboplastin time suggested the presence of coagulopathy, although the platelet count, PT/INR, fibrinogen level, and D-dimer test were not conducted, making it impossible to score SIC and DIC. The renal function tests revealed normal serum creatinine and electrolyte levels, but because serial creatinine levels were unavailable, progression to AKI was ruled out.

The arterial blood gas (ABG) obtained during the initial examination showed acidaemia, increased pCO2 and pO2, a base deficit of -4, and a normal bicarbonate level, suggesting respiratory and metabolic acidosis. The second ABG result, obtained close to the time of death, showed alkalotic pH, dangerously low pO2 (with an oxygen saturation of only 70%), high bicarbonate, and a base excess of +5.5. This means that there was a mixed metabolic alkalosis with severe hypoxemia due to terminal multi-organ dysfunction with advanced pulmonary decompensation.

3.3. Differential Diagnosis of Sepsis Source

Differential diagnosis in relation to the cause of septic shock at presentation consisted of four main factors: (1) a catheter-associated UTI, due to the presence of purulent urination along with urinary catheterization; (2) an infection arising at the site of surgery, which included infection related to the laminectomy done at T3-T4 20

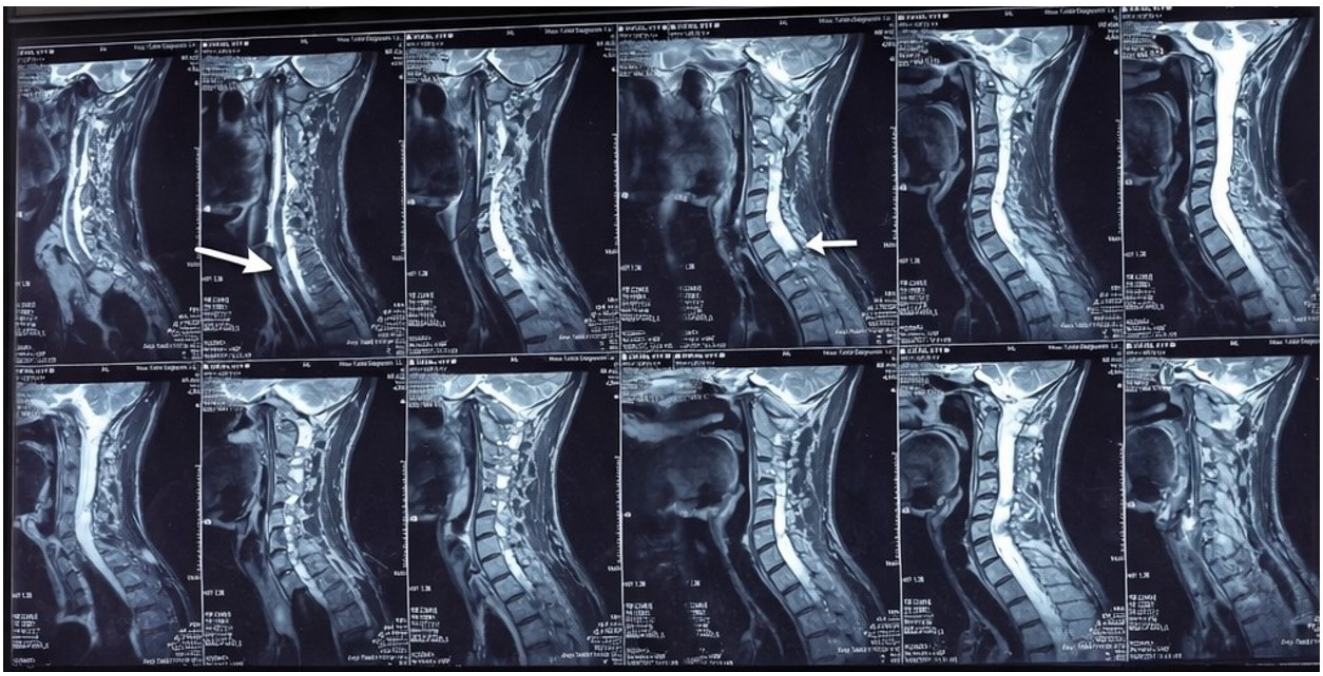

Figure 1: Sagittal T2-weighted magnetic resonance imaging (MRI) of the cervicothoracic spine demonstrating long-segment intramedullary signal change extending from the cervicomedullary junction to T11 (upper arrow), with cystic expansion of the cord and multiple intramedullary nodules consistent with hemangioblastomas (lower arrow).

days back or involving the area deeper than the skin; (3) a hospital-acquired or aspiration pneumonia because of orotracheal intubation in the context of significant neurological injury; and (4) a central venous catheter-associated bloodstream infection. In the absence of cultures of urine and blood, and any cross-sectional images or chest X-ray, a definitive determination of the source was not possible; a urological source seemed most likely, given purulent urination.

3.4. Imaging Findings

The previous CT angiography of the peripheral vascular system revealed several dilated and tortuous vessels of the spinal cord at the T2 level, supplied by the anterior and posterior spinal arteries, and an intramedullary enhancing nodule at T5, which were indicative of spinal hemangioblastoma with its associated vascular structure. The actual radiology report from the above examination was not accessible for inclusion in this case study. Another possibility, ependymoma, remained a consideration in the differential diagnosis.

The patient had a right renal corticomedullary cyst on ultrasound examination. No dimensions, complexity grading, or Bosniak category was stated; hence, this abnormality may be considered one of the visceral manifestations of VHL disease, although it cannot be taken to have any diagnostic value without more information.

MRI examination of brain and spine revealed bilateral phthisis bulbi with abnormal signal intensity; an enhancing mass lesion of the right eye 1.78 × 1.6 cm was noted, though pathology could not be determined. The seventh and eighth cranial nerves were within normal range. An intramedullary lesion extending from the posterior medulla of the cervicomedullary junction down to the T11 level was found. Nodular enhancement lesions were seen on the cystic cord expansion from C1 – C2 level (1.5 × 1.0 cm), C2 – C3 level (6 × 4 mm), and C4 level (1.8 × 1.6 cm). Mass effect of posterior medullary lesion of 1.5 × 1.6 × 2.4 cm size was exerted on the fourth ventricle, leading to ventricular dilatation and mild transependymal CSF exudation consistent with obstructive hydrocephalus.

An additional enhancing lesion within the left cerebellar hemisphere was noted as well. Based on the entire imaging appearance, namely the presence of multiple enhancing nodules with cystic degeneration in the spinal cord, the findings were compatible with VHL-related multifocal hemangioblastomas. Still, another possible differential diagnosis was also considered: ependymoma **(Figure 1)** and **(Figure 2)** .

VHL visceral studies, consisting of adrenal and pancreatic scanning and catecholamine study for pheochromocytoma, were not done due to the urgency of the case. Assessment for endolymphatic sac tumor was likewise not done.

3.5. Clinical Course and Outcome

The empirical therapy of broad-spectrum antibiotics, including IV piperacillin-tazobactam, was started based on the diagnosis of catheter-associated UTI leading to septic shock. Previous history of antibiotic exposure, laboratory data from microbial cultures, and possible acquisition of health care-associated pathogens were unknown.

Resuscitation of the patient's hemodynamics began with the administration of 1 L of normal saline intravenously, followed by norepinephrine infusion. During the following 72 hours, vasopressor therapy was increased with the use of the maximum dosage of dobutamine and dopamine. The dosing was done in drops per minute; thus, it was impossible to compare dosages using target values for weight-adjusted dosages. Targets for mean arterial pressure and fluid balance information were unavailable. Renal and liver dysfunction was not tracked on the trend chart. On the fourth day of hospitalization, progressive hemodynamic deterioration ensued.

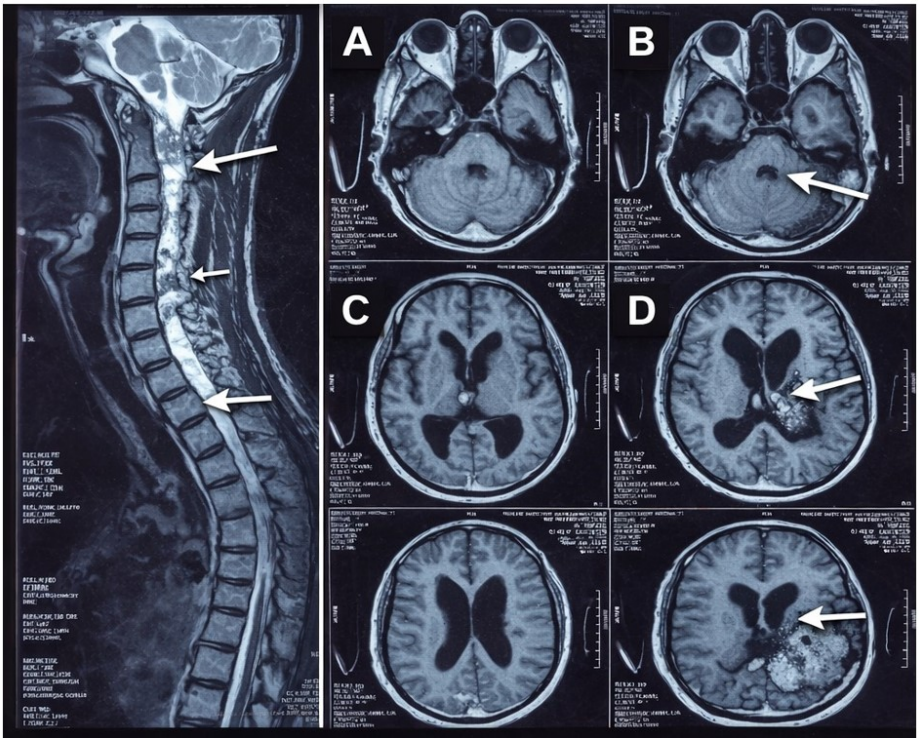

Figure 2: Composite MRI panel demonstrating intracranial and spinal cord findings. (A) Axial T2-weighted brain MRI at the level of the posterior medulla demonstrating an intramedullary lesion producing mass effect on the fourth ventricle with upstream obstructive hydrocephalus (arrow). (B) Axial T2-weighted brain MRI at the pontomedullary level demonstrating an intramedullary lesion (arrow). (C) Axial T2-weighted brain MRI demonstrating a lesion in the left cerebellar hemisphere with surrounding signal change (arrow). (D) Sagittal T2-weighted spine MRI demonstrating the longitudinal extent of the intramedullary lesion with associated enhancing nodules (arrow). All images were acquired at the index presentation and have been de-identified. Panel (D): sagittal spine; panels (A) – (C): axial brain

As a result of a refusal by the patient's family for CPR or escalation of therapy after four days, death occurred from septic shock with multi-organ failure. Based on the presentation of the patient's neurological deficits that were worsening, the initial infection is suspected to be urological in nature.

Given the comprehensive analysis of all relevant medical records and the history provided, a retrospective clinical diagnosis of VHL syndrome was suggested according to the clinical criteria set forth by Melmon and Rosen (1964) and updated by Binderup et al. (2022) [6, 7]. Testing for mutations in the VHL gene was not performed.

4. Discussion

In the current case, the patient's clinical profile was indicative of clinically diagnosed VHL syndrome. This diagnosis was made posthumously based on clinical criteria, although it took many years for him to develop symptoms. Three main aspects should be considered: first, the immediate cause of death, which was sepsis due to multi-organ dysfunction associated with a suspected urological origin; second, the contributory effect of neurological disability, caused by the growth of hemangioblastomas within the brainstem and spinal cord and leading to dependence on a catheter and thus to urological infection; and third, the problem of delayed syndromic diagnosis, which could have affected the natural history of the neurological disease.

The presumptive diagnosis for the source of urological sepsis was made in light of the presence of purulent urine in a patient with chronic catheterization. However, various potential sources of infection coexisted at the same time, such as the T3-T4 laminectomy that was conducted 20 days earlier, which posed the risk of postoperative wound infection, deep spinal infection, or infection related to an implanted device; hospital-acquired pneumonia or aspiration pneumonia secondary to recent orotracheal intubation along with neurological dysfunction; and bloodstream infection secondary to the presence of a central venous catheter. Given the absence of culture tests, imaging studies, and radiologic evidence, it may be prudent not to attribute the origin of sepsis to the urinary tract and label it urosepsis.

The timeline of retinopathy becomes paramount in the discussion of the diagnostic process. Retinal hemangioblastomas bilaterally at an early age are the hallmarks of VHL syndrome [17, 18]. Left globe enucleation at around age 10 years, right eye ocular involvement, and bilateral phthisis bulbi can be linked with the predicted pattern of a long-standing, severe case of bilateral retinal hemangioblastoma with associated glaucoma; even though there were no retinal hemangioblastoma pathology reports during the initial presentation, this case history plays a vital role in the diagnostic approach retrospectively. Lensectomy at 20 years of age is not part of the standard signs of VHL syndrome but is a possible complication due to long-standing intraocular pressure.

The hemangioblastomas of the spinal cord were large and included enhancing intramedullary nodules ranging from the cervicomedullary junction to T11. The presence of multifocal nodules, a cystic cord lesion surrounding them, and posterior medullary involvement causing obstructive hydrocephalus are features of VHL-associated multifocal hemangioblastoma. However, ependymoma cannot be ruled out without histological or molecular analysis.

Quadriplegia developing over a period of three years, which eventually led to the development of neurogenic bladder and the need for catheterization, was the crucial consequence of the spinal and brainstem hemangioblastomas. Therefore, the way the spinal cord hemangioblastomas caused death was indirectly through neurological deficits and the need for catheterization.

The detection of the right renal cortico-medullary cyst in abdominal ultrasonography can be considered an additional possible visceral manifestation of VHL syndrome. However, it is worth mentioning that the presence of simple renal cysts is frequent among subjects who are 40 years old or above and do not suffer from VHL syndrome, so caution should be observed while interpreting this result due to the lack of information concerning its size and the Bosniak Classification, as well as the absence of any renal mass or RCC. A thorough evaluation of visceral involvement in VHL syndrome, which would have included testing for adrenal, pancreatic, and catecholamine abnormalities, was not possible due to the acute nature of the case and its rapid progression.

Hepatitis C infection, identified during the patient's third decade of life, constitutes an important comorbidity within the framework of septic shock. No details were provided on viral load, stage of hepatic fibrosis, liver function test results, or immunosuppression. The degree to which HCV played a role in the severity or progression of septic shock remains unknown based on current information.

This delay in diagnosing what appears to be VHL syndrome, identified after the fact, could be explained by multiple factors operating at the systemic level. First, there were the issues of poor access to genetic counseling and hereditary cancer screening services, lack of multidisciplinary monitoring, and limited access to germline testing at the institution where the patient received care for many years. Furthermore, there was never any record suggesting that cascade testing, genetic counseling, and referral of the patient as a syndrome suspect had been conducted before, despite the reported family history of tumors in the retina, brain, and kidneys. This family history, including a sibling with an occipital brain tumor, another sibling with vision loss associated with tumors, and a parent with a kidney tumor, was established according to the patient's self-report.

The drug Belzutifan, which was granted FDA approval in 2021 for the treatment of non-surgical VHL-associated central nervous system hemangioblastomas [15, 16], is briefly mentioned here as a contemporary treatment option for VHL syndrome. It should be noted that this therapy is dependent on molecular diagnosis, clinical indication, and a level of clinical stability not present in the acute context of this case.

5. Limitations

Some of the major limitations of this case presentation include the lack of histopathological investigation of the lesion excised and the lack of germline testing of the VHL gene; as a result, the diagnosis of VHL remains purely clinical, and the possibility of ependymoma cannot be ruled out. Documented records did not support the patient's initial retinal diagnosis. Data such as microbiology results, urine cultures, blood cultures, and sensitivities could not be obtained to help determine the source of the infection and the causative organism. Information regarding the ICU management, coagulation profile, HCV viral loads, and hepatic involvement could not be obtained.

6. Conclusion

In this report, the patient has a medical history that suggests clinically diagnosed VHL syndrome, with no need for genetic analysis or histopathology, as the diagnosis was made postmortem based on clinical parameters. The leading cause of death is sepsis with organ dysfunction due to an infection of undetermined microbial origin involving a urological source. The significant risk factor for mortality in this case is urinary catheterization due to neurological deficits caused by multiple hemangioblastomas in the spinal cord and brain stem that have not been medically addressed. This report highlights the significance of hemangioblastomas, particularly bilateral or early-onset retinal involvement, in the diagnosis of hereditary cancer syndromes. When resources are available, family genetic screening in accordance with clinical guidelines is recommended.

Conflicts of Interest

The authors declare no conflicts of interest.

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None.

Ethical Approval and Patient Consent

Informed written consent for publication was obtained from the patient's next of kin. The institutional review board waived ethical review in accordance with institutional policy for retrospective single case report publications. Ethical Approval is not required for case reports at our institution. Patient data have been de-identified in accordance with institutional privacy requirements.

Large Language Model

None.

Author Contributions

TK, HWS, and STH contributed to data collection and case selection. AMB, MHJ, and AHK contributed to references, reviewing, and editing. AI and SAK contributed to writing the original draft. NUI and AA contributed to patient follow-up, obtaining consent, editing, reviewing, and formatting. All authors read and approved the final manuscript.

Data Availability

None.

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